MEG source localization in extratemporal epilepsy

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1 Introduction

Although patients suffering from medically intractable epilepsies originating from other than the temporal lobe are less numerbale than those with temporal lobe epilepsies (TLE), localization of the epileptogenic region in extratemporal epilepsies (ETE) is considered as much more demanding than in TLE [1, 2]. Even if seizure semiology may hint at the origin in specific parts of the brain [3-7], non pathologic imaging data and propagational features with fast spreading of epileptic activity to and from frontal areas may impede identification of the epileptogenic region.

In addition to localization of focal epileptic activity, preoperative evaluation of ETE surgery candidates requires delineatin of sensory, motor, and speech related areas and their mutual relationships with the epileptogenic zone.

In order to achieve this difficult localizational task, invasive recording from intracranial electrodes is often required, adding considerable strain and risk to presurgical evaluation. Therefore, the introduction of magnetoencephalography (MEG) as a noninvasive electrophysiological method with promising localizing features [8-13] offered a welcome new dimension to epileptic focus localization.

The growing sophistication of analysing tools such as spatiotemporal analyses [14, 15], multiple source estimates [16, 17], and detailed evaluation of propagational features [14] has had its share in the improvement of MEG's clinical relevance in the ETE field, as well as hardware developments.

We present examples of MEG localizations in ETE patients to illustrate some aspects of MEG contribution to successful presurgical evaluation in this challenging field.

2 Patients and methods

Approximately one fourth out of 222 patients with refractory epilepsy who underwent presurgical evaluation at the Erlangen epilepsy center who were investigated with MEG during the last decade, suffered from ETE (n = 69; 45 men, 24 women; age 8 to 58; mean age 30 years). Most of these (55, approx. 80%) had frontal lobe foci.

2.1 Recording procedures

Two biomagnetic systems with axial first order gradiometers, operated in a magnetically shielding chamber (Vakuumschmelze, Hanau, Germany) were used in succession to obtain MEG data (1. Krenikon®, Siemens, Erlangen, Germany, and 2. Magnes II®, 4-D Neuroimaging, San Diego, CA, USA).

The first device had 37 sensors arranged in a planar array of 19 cm diameter, suitable for one hemisphere recordings. The second system featured two sensor units with 37 channels each, the sensors set in concave arrays of 14 cm diameter and designed for simultaneous MEG recording from both hemispheres. A 32 channel EEG amplifier was additionally used, specifically built for simultaneous MEG and EEG recordings (Schwarzer, München, Germany).

For the purpose of visualizing MEG localization results in anatomically correct brain images, MEG was merged with MRI data (magnetic source imaging, MSI). A common 3-dimensional coordinate system was established by either using patients‘ individual dental impressions or reference points on the patients' head, with appropriate documentation in both MEG and MRI settings.

EEG was simultaneously recorded with MEG in 15 of the ETE patients, using caps and electrodes particularly designed for use in the MEG environment (Falk Minow, München, Germany). Generally, one ECG channel was recorded in order to detect artifacts in MEG traces due to magnetic heart activity.

MEG and EEG were recorded with bandpass filtering of 1-100 Hz and a 500 Hz sampling rate. Patients were comfortably positioned on an adjustable bed, with the head placed in a fixed position either by closing the mouth around the dental impression, or by a vacuum cast.

2.2 Evoked cortical responses

Somatosensory evoked magnetic fields (SEF) were obtained by (a) slight pushes of air pressure driven plastic membranes applied to finger tips or (b) electrical median nerve stimulation. SEF were averaged from 200 single trials each.

For recording of speech related evoked fields [18], target (meaningful), and non-target (meaningless) stimuli were visually presented. Stimuli were (a) four letter strings or (b) line drawings and had to be (a) silently read or (b) named. A 0.1 Hz high pass filter was used; series consisted of 300 stimuli. Eye movements, as a potential source of artifacts, were additionally recorded. Target and non-target epochs were separately averaged and the result of the meaningless condition subtracted from the response to meaningful stimuli.

2.3 Procedures of analysis

2.3.1 Standard procedures

Generally, specific epileptic MEG signals (single spikes and averages, if applicable) and main SEF peaks were localized by means of dipole calculation, based upon the model assumptions of an equivalent current dipole (ECD) in a homogeneously conducting sphere. Best fitting dipoles ($c <.98$, with $c =$ correlation between empirical and calculated dipolar distribution) were displayed in the corresponding MRI slices.

2.3.2 Additional procedures

Hitherto, ten selected cases were evaluated using more sophisticated procedures including multiple dipole fit, current density reconstruction (minimum norm least square fit) and realistically shaped volume conductors according to the boundary element method (BEM), with the compartments skin, skull being set up from T1-weighted MRI data using standard values for the conductivities [19, 20]. As these analyses were also applied to the EEG data, the realistic head conductor model was particularly required [21, 22]. In three cases, the combined MEG and EEG data sets [20, 23] were analysed.

Speech related evoked magnetic fields were analysed by means of the CLSF software, a current density algorithm [18, 24]. Latencies yielding results in Broca's area approximatly 350 msec, those pertaining to Wernicke's area were in the range of 500 msec.

3 Results

3.1 Reproducibility of MEG localizations

The patient, a young man whose MRI scans revealed a slight structural abnormality in the left frontal lobe, suffered from seizures characterized by motor symptoms in his right hand and arm, occasionally accompanied by impaired sensitivity. During a period of over two years, when several regimens of antiepileptic medication were tried, repeated MEG recordings were performed. Localization results of all three investigations clustered around the posterior part of the lesion, showing good reproducibility of repeated measurements. In addition, SEF localizations after mechanical finger tip stimulation were found to be symmetrical, and set apart from the region of epileptic activity.

3.2 MEG localization with respect to a large frontal lobe lesion

The young female patient, after tumour surgery, presented with a lesion in her MRI scans and according symptomatic epilepsy. MEG results revealed a clear cut source of epileptic discharges at the anterolateral border of the large resection cavity. Invasive electrostimulation and EEG recordings confirmed the generation of focal epileptic activity within the motor strip. These findings supported the decision to apply multiple subpial transsections (MST), from which the patient markedly benefitted.

3.3 Non-lesional case, guidance of subdural grid placement by MEG findings

In contrast to the first two cases, this patient's MRI scans were normal. Although routine noninvasive findings suggested seizure origin in the left frontal lobe, results were not ultimately conclusive. Thus, intracranial EEG recording was considered. MSI, performed prior to grid implantation, indicated epileptic spikes to originate from the base of the left frontal lobe. Subdural grid placement was planned accordingly, and invasive recordings confirmed MSI results. The subsequent resection yielded seizure control.

3.4 MEG localization of specific epileptic and functional data; combined MEG/EEG results

Recurrence of a large cyst in the left frontal lobe caused symptomatic epilepsy in this young man. Interictal and ictal findings from video-EEG monitoring suggested seizure origin in the left fronto-temporal region. Localization based upon current density reconstruction from MEG indicated the area around the lesion to generate epileptic activity. Dipole analyses of simultaneously recorded MEG and EEG data were computed for the separate as well as for the combined data sets, with MEG spikes having to be used as trigger signals for identification of the respective EEG patterns. Dipole sites clustered at the upper margin of the lesion. Results from MEG and the merged data set were most clear-cut than those from EEG.

Analysis of language related evoked magnetic fields revealed Broca's area to be distinctly different from the focal area, its location bordering the lower margin of the cyst.

Intraoperative ECoG confirmed MSI findings; the patient is seizure free after surgery (see fig. 1).

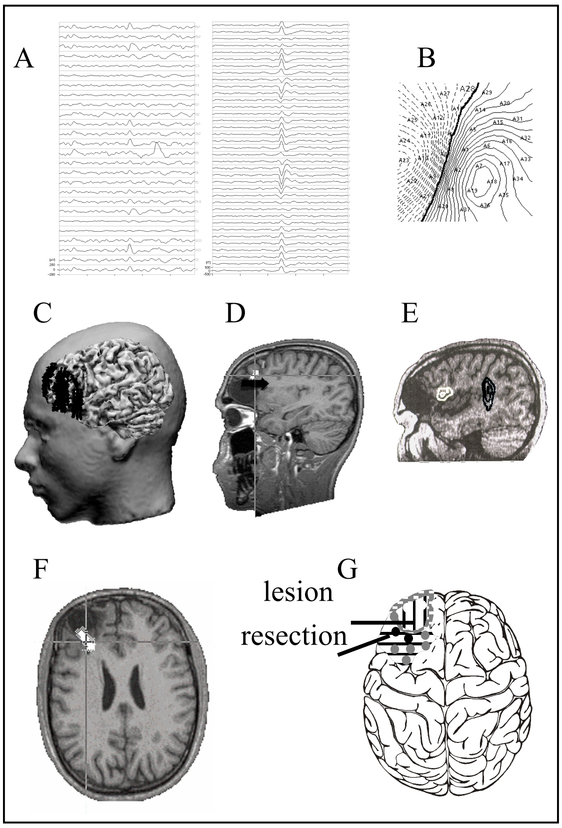

Figure 1: *Illustration of case 3.4. (A) Averaged EEG and MEG spikes, (B) MEG map during rising spike slope, (C) skin and cortex compartments with result of current density reconstruction from MEG, (D) sagittal MRI slice with MEG (black arrows) and EEG (white arrows) dipole results, (E) Broca's (white lines) and Wernicke's (black lines) areas, (F) dipole sites from MEG analysis (white arrows), (G) schematic sketch of intraoperative situation. Circles: ECoG electrodes; white: no spikes, grey: few spikes, black: maximum spiking.*

3.5 Symptomatic epilepsy of the parieto-occipital region

After removal of a cavernoma in the left parieto-occipital region, and with another one remaining in the occipital lobe, the patient presented again, with insufficiently reduced seizure frequency. Whereas surface EEG and ictal SPECT yielded merely lateralizing results, MSI revealed residual epileptic activity bordering the resection site. As the patient happened to have a seizure during MEG recording, ictal data was additionally analysed. Current density reconstruction showed a circumscribed area of early ictal activity around the resection cavity, and subsequent dipole analysis yielded results congruent with that from interictal data.

4 Conclusion

From a long standing experience with MSI localizations in patients undergoing presurgical evaluation of ETE and the application of different methods of analysis we conclude that MSI contributes to the delineation of focal epileptic activity by particularly narrowing down the scope of lateralization and lobe identification to confined centers of activity.

Thus, it facilitates detailed planning of both operative and diagnostic neurosurgical procedures. The minute relationship between lesion and epileptogenic region may be established in order to precisely devise extent of resection. In non-lesional cases, a restrained design of intracranial electrode placement can be achieved.

Furthermore, the contribution of MSI to determine the exact spatial relationships between centers of epileptic activity and functionally (somatosensory, motor, speech, visual) significant areas has proven highly valuable.

The use of wholehead biomagnetic systems [25-29] with their advantage of shorter recording sessions, inclusion of simultaneously recorded EEG into localizing routines in order to increases the yield of both MEG and EEG investigations[20, 22, 30-35], and the implementation of MEG/EEG localization results into neuronavigation systems [36] are aspects for further improvement of MEG exploration in ETE.

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References

1. R.N. Harner and S. Riggio, "Interictal EEG topography of frontal lobe epilepsy", *Adv.Neurol.* **57,** 331-338, 1992.
2. P. Kotagal and G.S. Arunkumar, "Lateral frontal lobe seizures", *Epilepsia* **39** (Suppl 4**),** 62-68, 1998.
3. P. Chauvel, F. Kliemann, J.P. Vignal, J.P. Chodkiewicz, J. Talairach, and J. Bancaud, "The clinical signs and symptoms of frontal lobe seizures. Phenomenology and classification", *Adv.Neurol* **66,** 115-125, 1995.

4. P.D. Williamson, "Frontal lobe epilepsy. Some clinical characteristics", *Adv.Neurol* **66,** 127-150, 1995.
5. H.G. Wieser and M. Hajek, "Frontal lobe epilepsy. Compartmentalization, presurgical evaluation, and operative results", *Adv.Neurol* **66,** 297-318, 1995.
6. P.D. Williamson, P.C. Van Ness, H.G. Wieser, and F. Quesney, "Surgically Remediable Extratemporal Syndromes", in *Surgical Treatment of the Epilepsies,* J. Jr. Engel, Ed. New York: Raven Press. 1993, pp. 65-76.
7. H. Stefan, "Epilepsien: Diagnose und Behandlung", Stuttgart: Georg Thieme Verlag. 1999
8. M. Hämäläinen, R. Hari, L. J. Ilmoniemi, J. Knuutila, and O.V. Lounasmaa, "Magnetoencephalography - theory, instrumentation, and applications to noninvasive studies of the working human brain", *Reviews of Modern Physics* **65,** 413-497, 1993.
9. M.S. Hämäläinen, "Basic principles of magnetoencephalography", *Acta Radiol.Suppl.* **377,** 58-62, 1991.
10. H. Stefan, S. Schneider, K. Abraham Fuchs, J. Bauer, H. Feistel, G. Pawlik, U. Neubauer, G. Rohrlein, and W. J. Huk, "Magnetic source localization in focal epilepsy. Multichannel magnetoencephalography correlated with magnetic resonance brain imaging", *Brain* **113,** 1347-1359, 1990.
11. H. Stefan and C. Hummel, "Magnetoencephalography", in *Handbook of Clinical Neurology,* H. Meinardi, Ed. Amsterdam: Elsevier. 1999, pp. 319-336.
12. C. Baumgartner and L. Deecke, "Magnetoencephalography in clinical epileptology and epilepsy research", *Brain Topogr.* **2,** 203-219, 1990.
13. J.S. Ebersole, "Magnetoencephalography / magnetic source imaging in the assessment of patients with epilepsy", *Epilepsia* **38** (Suppl 4), 1-5, 1997.
14. M. Scherg, T. Bast, and P. Berg, "Multiple source analysis of interictal spikes: goals, requirements, and clinical value". *J Clin Neurophysiol* **16,** 214-224, 1999.
15. D. P. Schwartz, J. M. Badier, P. Bihoue, and A. Bouliou, "Evaluation of a new MEG-EEG spatio-temporal localization approach using a realistic source model", *Brain Topogr.* **11,** 279-289, 1999.
16. J.C. Mosher, S. Baillet, and R.M. Leahy, "EEG source localization and imaging using multiple signal classification approaches", *J. Clin. Neurophysiol.* **16,** 225-238, 1999.
17. T. D. Waberski, H. Buchner, K. Lehnertz, A. Hufnagel, M. Fuchs, R. Beckmann, and A. Rienacker, "Properties of advanced head modelling and source reconstruction for the localization of epileptiform activity", *Brain Topogr.* **10,** 283-290, 1998.
18. M. Möller, H. Kober, O. Ganslandt, C. Nimsky, J. Vieth, and R. Fahlbusch, "Functional mapping of speech evoked brain activity by magnetoencephalography and its clinical application", *Biomed.Tech.Berlin.* **44,** 159-161, 1999.
19. M. Fuchs, R. Drenckhahn, H.A. Wischmann, and M. Wagner, "An improved boundary element method for realistic volume-conductor modeling", *IEEE Trans.Biomed.Eng.* **45,** 980-997, 1998.
20. M. Fuchs, M. Wagner, H.A. Wischmann, T. Kohler, A. Theissen, R. Drenckhahn, and H. Buchner, "Improving source reconstructions by combining bioelectric and biomagnetic data", *Electroencephalogr.Clin.Neurophysiol.* **107,** 93-111, 1998.
21. H. Buchner, T.D. Waberski, M. Fuchs, H.A. Wischmann, M. Wagner, and R. Drenckhahn, "Comparison of realistically shaped boundary-element and spherical head models in source localization of early somatosensory evoked potentials", *Brain Topogr.* **8,** 137-143, 1995.
22. F. H. Lopes da Silva, H. J. Wieringa, and M. J. Peters, "Source localization of EEG versus MEG: empirical comparison using visually evoked responses and theoretical considerations", *Brain Topogr.* **4,** 133-142, 1991.
23. R. E. Greenblatt, "Combined EEG/MEG source estimation methods", in *Biomagnetism: Fundamental Research and Clinical Applications,* C. Baumgartner, L. Deecke, G. Stroink, and and S.J. Williamson, Eds. Vienna: Elsevier. 1995, pp. 402-405.
24. S.E. Robinson and D.G. Rose, "Current source image estimation by spatially filtered MEG", in *Biomagnetism: Clinical Aspects,* G. Hoke, S. Erne, Y. Okada, and G.-L. Romani, Eds. Amsterdam: Elsevier . 1992, pp. 761-765.
25. R. Paetau, M.-L. Granström, G. Blomstedt, V. Jousmäki, M. Korkman, and E. Liukkonen, "Magnetoencephalography in Presurgical Evaluation of Children with the Landau-

Kleffner-Syndrome". *Epilepsia* **40,** 326-335, 1999.

26. M.S. Hämäläinen, "Functional localization based on measurements with a whole-head magnetometer system", *Brain Topogr.* **7,** 283-289, 1995.
27. N. Nakasato, K. Seki, T. Kawamura, S. Ohtomo, A. Kanno, S. Fujita, K. Hatanaka, S. Fujiwara, T. Kayama, A. Takahashi, H. Jokura, T. Kumabe, H. Ikeda, K. Mizoi, and T. Yoshimoto, "Cortical mapping using an MRI-linked whole head MEG system and presurgical decision making", *Electroencephalogr.Clin Neurophysiol Suppl.* **47,** 333-341, 1996.
28. O.V. Lounasmaa, M.S. Hämäläinen, R. Hari, and R. Salmelin, "Information processing in the human brain: magnetoencephalographic approach", *Proc.Natl.Acad.Sci.U.S.A.* **93,** 8809-8815, 1996.
29. R. Hari, A. Ahonen, N. Forss, M.L. Granström, M.S. Hämäläinen, M. Kajola, J. Knuutila, O.V. Lounasmaa, J.P. Mäkelä, and R. Paetau, "Parietal epileptic mirror focus detected with a whole-head neuromagnetometer", *Neuroreport* **5,** 45-48, 1993.
30. P. Ossenblok, G. Wilts, J. Numminen, M.J. Peters, and F. H. Lopes da Silva, "Locating the cortical sources of somatosensory evoked responses by integration of EEG and MEG", in *Functional Neuroscience,* C. Barber, G. Celesia, G. C. Comiand F. Mauguiere, Eds. Amsterdam: Elsevier Science B.V. 1996, pp. 183-191.
31. M. Scherg and H. Buchner, "Somatosensory evoked potentials and magnetic fields: separation of multiple source activities", *Physiol.Meas.* **14** (Suppl 4A)**,** A35-39, 1993.
32. H. Stefan, S. Schneider, H. Feistel, G. Pawlik, P. Schuler, K. Abraham Fuchs, T. Schlegel, U. Neubauer, and W. J. Huk, "Ictal and interictal activity in partial epilepsy recorded with multichannel magnetoelectroencephalography: correlation of electroencephalography/ electrocorticography, magnetic resonance imaging, single photon emission computed tomography, and positron emission tomography findings", *Epilepsia* **33,** 874-887, 1992.
33. W.W. Sutherling, M.F. Levesque, P.H. Crandall, and D.S. Barth, "Localization of partial epilepsy using magnetic and electric measurements", *Epilepsia* **32** (Suppl 5)**,** 29-40, 1991.
34. J.S. Ebersole, W. Haven, and M. Scherg, "Spike Focus Localization Using Dipole Models from Simultaneous MEG and EEG", *Neurology* **44,** 1994.
35. H. Stefan, C. Hummel, S. Schneider, R. Meyrer, K. Abraham-Fuchs, P. Schüler, U. Neubauer, and W. J. Huk, "Multi-channel Magnetoelectro-encephalography", in *Focus Localization,* G. Pawlik and H. Stefan, Eds. Berlin: 1996, pp. 247-259.
36. O. Ganslandt, R. Fahlbusch, C. Nimsky, H. Kober, M. Moller, R. Steinmeier, J. Romstock, and J. Vieth, "Functional neuronavigation with magnetoencephalography: outcome in 50 patients with lesions around the motor cortex", *J Neurosurg.* **91,** 73-79, 1999.